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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,968	02/20/2004	Kevin J. Williams	W1107/20009	9607

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/782,968	WILLIAMS, KEVIN J.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *241,242,244,245,248-253,256 and 265-316* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41,242,244,245,248-253,256 and 265-316* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the species election requirement in the reply filed on December 5, 2008 is acknowledged. The traversal is on the ground(s) that "...different search strategies are not required...", see Remarks, page 4, 1st full paragraph. The Examiner has reconsidered the election of species and Applicant's traversal has been found persuasive.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 265-316 are pending.

Claims 1-240, 243, 246, 247, 251, 254, 255 and 257-264 have been cancelled.

Claims 265-316 have been added.

Claims 241, 242, 244, 245, 248-250, 253 and 256 have been amended.

Claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 265-316 are examined on the merits.

Claim Objections

3. Claim 274 is objected to because of the following informality: the claim does not end with a period, hence it is not clear if additional text is missing. Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 309-316 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION**.

Applicant has added claims 309-316 that introduce new matter. Specifically, claim 309 reads on a method wherein a first binding agent is implemented to quantitate a total, thrombospondin plus either the thrombospondin fragment(s) and a second binding agent is used to quantitate thrombospondin only. The claim further establishes using the difference between the quantitations as a quantitation of the amount of thrombospondin fragment or fragments.

The specification cites on page 18, lines 7-13,

> "In a third approach, the assay distinguishes the fragment (or fragments) based on one or more epitopes in thrombospondin that are not present in the fragment. As an illustrative but not restrictive example, *an epitope shared by thrombospondin and a thrombospondin fragment is used to obtain a quantitation of a total, thrombospondin plus thrombospondin fragment(s), from which is then subtracted a quantitation of thrombospondin obtained using an epitope present in thrombospondin but not present in a fragment.* The difference between the two quantitations is a quantitation of the amount of fragment. "

This section of the specification is remiss of binding agents and depends on detecting *epitopes* on thrombospondin and/or thrombospondin fragment(s). The pending claims are broader than what is set forth in the specification. Applicant does not have support for these new claims and should delete the new matter or pointedly express in the specification by page and line number where support is found.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 241, 242, 244, 245, 248-253, 256 and 265-316 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 241, 249, 276, 289, 297, 303 and 309 are vague and indefinite because these claims recite an individual's plasma level of thrombospondin fragment or fragments is used in a diagnosis, wherein the plasma level is greater and if so it is implicative of the individual has a neoplastic disease. However, there is no comparison step listed in the claims clarifying what level the individual's plasma level should be greater than. It is not clear what plasma level of thrombospondin denotes neoplastic disease and what this level is compared to. The metes and bounds of the claims cannot be determined.

b. Claims 276 and 312 are indefinite because they recite amino acid residues and corresponding position numbers, however there are no sequences or SEQ ID number information provided. The metes and bounds cannot be determined.

c. Claim 309 recites in the lines 3 and 4, "utilizing a first binding agent to obtain a quantitation of a *total*, thrombospondin plus either the thrombospondin fragment or fragments". It is not clear what product or molecule has been quantitated. Furthermore, it is not clear what product or molecule the term, total describes. Applicant is requested to clarify.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 241, 245, 248, 249, 253, 256 and 265-276 are rejected under 35 U.S.C. 102(b) as being anticipated by Jackowski et al./ U.S. Patent application publication number 2003/0119074 A1 (December 20, 2001). Jackowski

discloses a method of detecting immunological fragments of thrombospondin with an antibody or binding partner in a plasma sample, see abstract; page 3, section 0029; page 5, section 0065. Absent evidence to the contrary the molecular weight of said fragment or any of said fragments not exceeding 140 kDa, the molecular weight of said fragment or fragments being at least 20 kDa, wherein the size in kDa is that detemained by gel electrophoresis after disulfide bond reduction, and wherein the fragment or each of said fragments comprises a portion of thromobospondin selected from the group consisting of a collagen type V binding domain, and a domain or a part thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, an oligomerization domain, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat.

10. Claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 256-316 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number 2003/0166017 A1/ McCarthy (filed November 9, 2001). The publication discloses a method of assessing the level of a TSP fragment in plasma using an antibody or ligand, which reads on Applicant's active step of measuring an individual's plasma level of thrombospondin fragments, see page 2, section 0017; page 4, section 0059; page 5, section 0061; page 8, section 0095; page 9, sections 0096, 0099 and 0100; and page 10, section 0103. Moreover, the level of a TSP fragment or marker may be comparatively assessed, whereby the 'normal' level of TSP marker is determined and

compared to a patient sample, see page 5, section 0066. Absent evidence to the contrary the molecular weight of said fragment or any of said fragments not exceeding 140 kDa, the molecular weight of said fragment or fragments being at least 20 kDa, wherein the size in kDa is that detemained by gel electrophoresis after disulfide bond reduction, and wherein the fragment or each of said fragments comprises a portion of thromobospondin selected from the group consisting of a collagen type V binding domain, and a domain or a part thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, an oligomerization domain, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 256-316 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/07035 (published 19 February 1998), and further in view of U.S. Patent Application Publication number 2003/0166017 A1/ McCarthy (filed November 9, 2001).

The WO document teaches antibodies that detect thrombospondin fragments (collectively referred to as "ADP") in a body fluid, see abstract; bridging paragraph of pages 11 and 12. The antibodies cross-react with 67-80 kDa and 20kDa fragments of thrombospondin-1, see page 7, 2nd paragraph; and page 9, 1st full paragraph. Absent evidence to the contrary the fragment or each of said fragments comprises a portion of thromobospondin selected from the group consisting of a collagen type V binding domain, and a domain or a part thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, an oligomerization domain, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat. The WO document does not teach the comparison of amounts of TSP fragment plasma levels between two individuals.

However, McCarthy teach a method of assessing the level of a TSP fragment in plasma using an antibody or ligand, which reads on Applicant's active step of measuring an individual's plasma level of thrombospondin fragments, see page 2, section 0017; page 4, section 0059; page 5, section 0061; page 8, section 0095; page 9, sections 0096, 0099 and 0100; and page 10, section 0103. Moreover, the level of a TSP fragment or marker may be comparatively assessed, whereby the 'normal' level of TSP marker is determined and compared to a patient sample, see page 5, section 0066. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of both the WO document and McCarthy because they both read on the applicability of measuring TSP for the

assessment of disease. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings the references that monitoring and evaluating the TSP markers are a must for diagnosing a diseases state and consequently establishing the proper cancer management and assessing the benefits of a particular treatment regimen.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 256-316 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 163, 164, 166-168 and184-193 of

copending Application No. 10/419,462 (filed February 20, 2004). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of both applications share the active method step of measuring an individual's plasma level of thrombospondin fragment or fragments with a binding agent in order to detect the presence and/or clinical course of a neoplastic disease.

15. Claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 256-316 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 67 and 168-182 of copending Application No. 10/525,610 (filed March 24, 2006). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of both applications share the active method step of measuring an individual's plasma level of thrombospondin fragment or fragments with a binding agent in order to detect the presence and/or clinical course of a neoplastic disease. And even though the copending application includes claims reading on a kit. The kit has no patentable weight and the said kit encompasses the claimed method measuring an individual's plasma level of thrombospondin fragment or fragments with a binding agent in order to detect the presence and/or clinical course of a neoplastic disease.

16. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone

number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, Monday through Saturday.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
02 March 2009
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643